Scientific Abstract

Central to the realization of the potential of virotherapy for malignancy is the ability to accomplish efficient and specific oncolytic virus delivery to targeted cancer cells of interest. To this end, investigators at University of Alabama at Birmingham (UAB) and MD Anderson have developed a novel infectivity enhanced conditionally replicative adenovirus (CRAD) designated Ad5-Δ24RGD. This targeted CRAD has been shown to selectively replicate in ovarian cancer cells and achieve dramatically enhanced anti-tumor activity in both *in vitro* and *in vivo* models of ovarian cancer. It is our hypothesis that by virtue of the enhanced tumor cell transduction achieved with this tropism-modified CRAD, an enhanced therapeutic effect in the context of a cancer virotherapy approach for carcinoma of the ovary, a disease in need of new therapeutic paradigms, will be realized. Accordingly, this proposal includes a human gene therapy protocol for ovarian and extraovarian cancer patients with persistent or recurrent disease. This Phase I protocol will 1) determine the maximally tolerated dose and spectrum of toxicities encountered with intraperitoneal delivery of Ad5-Δ24RGD in patients with recurrent ovarian cancer; 2) determine the biologic effects encountered with intraperitoneal delivery of Ad5-Δ24RGD in patients with recurrent ovarian cancer cells; and 3) determine immunologic response generated against Ad5-Δ24RGD when administered intraperitoneally to patients with recurrent ovarian adenocarcinoma. It is anticipated that the protocol described herein would establish the safety of this therapeutic and provide an indication of the efficacy of this approach in human subjects with ovarian cancer and allow the rapid evaluation of the clinical utility of this novel therapeutic in future Phase II/III trials.